HYDROGELATION OF CYCLIC PEPTIDE AMPHIPHILE, COLISTIN, THROUGH FORMATION OF HIERARCHICALLY ORGANIZED STRUCTURE

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Colistin (Col) is an cationic amphiphilic molecule having a cyclic peptide moiety as a hydrophilic group. Because of such a unique molecular architecture, self-assembled structure of Col should be much different from that of a linear amphiphilic peptide. Especially, effect of pH on self-assembly in aqueous Col solution is interesting because inter- and intra-ring interactions of Col should be affected with pH change. Thus, in this study, we investigated self-assembly of Col in aqueous solution with various pH by using small-angle X-ray scattering (SAXS) with synchrotron light source.

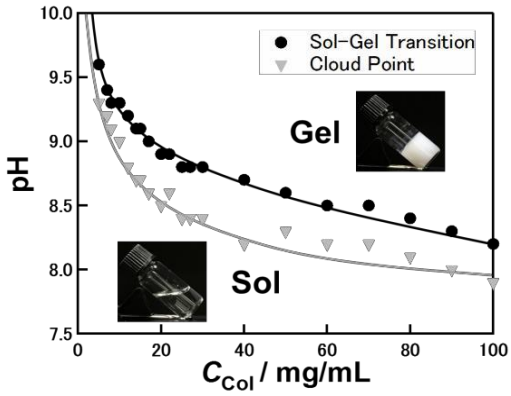

Figure 1 – Phase diagram of aqueous solution of Col in pH-C_{Col} plane

Figure 1 shows the phase diagram summarizing gel-sol states in pH-Col concentration (CCol) plane. Aqueous solution of Col forms sol above CMC and shows sol-to-gel transition in the region at high pH and CCol. The aqueous solution of Col micelle changes from transparence sol to turbid hydrogel with increasing pH. This result suggests that self-assembled structure of Col in aqueous solution is drastically changed with increasing pH. Since the Col has 5 cationic groups, the electrostatic repulsion between the amino groups should be strong at low pH, although the electrostatic repulsion should be weakened at high pH. The change in electrostatic interactions depending on pH should cause the self-assembled structure of Col.In order to investigate the self-assembled structure of Col in aqueous solution, small-angle X-ray scattering (SAXS) measurements were carried out at BL-40B2 of SPring-8, Japan.

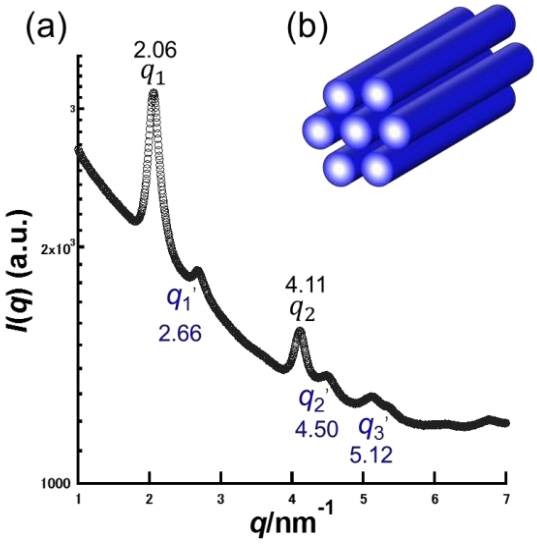

Figure 2 – (a) SAXS profile from aqueous solution of Col in gel situation (b) Schematic representation of hexagonally packed cylinder of Col molecules

SAXS measurements showed Col formed self-assembled dimer in transparent sol situation. On the contrary, in hydrogel situation, it was found out that Col forms fiber-like aggregates with hierarchically organized structure. Figure 2 (a) shows SAXS profiles of Col in aqueous solution at pH = 8.4. Here, the q is the magnitude of scattering vector defined by q = (4□/□) sin□ (2□□is scattering angle). SAXS profile was observed clear diffraction peaks. These peaks seem to be divided to two series. One is the diffractions from ordered lamellar structure, in which the peaks at q = 2.06 nm-1 and 4.11 nm-1 are the 1st and 2nd order peaks, respectively. From the q position of 1st order peak, the periodic length of the ordered lamellar structure is estimated to 3 nm. The other series is three peaks at q = 2.66, 4.50, and 5.12 nm-1. Since these peaks are relatively located at 1 : 31/2 : 2 against the q position of the peak at 2.66 nm-1. This pattern is ascribed to the hexagonally packed cylinder as shown in Figure 2 (b). Therefore, it should be considered that Col molecules hierarchically assemble into Cylinder-within-Lamellar structure in fiber like aggregates formed in gel situation. Since the formation of inter-ring hydrogen bonds between Col molecules are enhanced in high pH region, Col molecules should be arranged one dimensionally to form cylinders